Scanning Electron Microscopy

Volume 1986 | Number 4 Article 45

8-30-1986

# Phase Transitions of Calcium Oxalate Trihydrate and Epitaxy in the Weddellite-Whewellite System

Sergio Deganello
*University of Chicago*

SCANNING ELECTRON MICROSCOPY/1986/IV (Pages 1721-1728)
SEM Inc., AMF O'Hare (Chicago), IL 60666-0507 USA

0586-5581/86$1.00+05

# PHASE TRANSITIONS OF CALCIUM OXALATE TRIHYDRATE AND EPITAXY IN THE WEDDELLITE-WHEWELLITE SYSTEM

Sergio Deganello *

Nephrology Program, University of Chicago, IL
and Institute of Mineralogy, University of Palermo, Italy

(Received for publication April 07, 1986, and in revised form August 30, 1986)

## Abstract

The phase changes calcium oxalate trihydrate-weddellite, weddellite-calcium oxalate monohydrate and calcium oxalate trihydrate-whewellite are individually examined at the atomic level from a theoretical point of view; concomitantly the topological requirements necessary for phase stability are clarified for each structure type. In solution a sequential series of phase transitions according to the steps calcium oxalate trihydrate-weddellite-whewellite is not likely to be energetically favoured; direct conversion of calcium oxalate trihydrate to whewellite should be, instead, ordinarily expected.

It is formally demonstrated that along two axial directions a set of atoms is in essentially identical positions in both weddellite and whewellite. This notwithstanding, it is concluded that epitactic catalysis cannot and should not be considered a common mechanism for the formation of whewellite from weddellite (and vice versa) or of kidney stones in general.

Key words: Calcium oxalate trihydrate, weddellite, whewellite, crystal structures, calcium oxalate trihydrate-weddellite phase change, weddellite-whewellite phase change, calcium oxalate trihydrate-whewellite phase change, epitaxy, clinical relevance.

* Address for correspondence: SCL,Box 42, The University of Chicago,5735 S.Ellis, Chicago, IL 60637
Phone no.: (312) 962-7062

## Introduction

Only rarely is calcium oxalate trihydrate (COT) found in urine or in renal calculi. Nevertheless COT has received much attention (i.e., Gardner, 1975) due to the possibility that it may be a precursor to the formation of whewellite (COM) and weddellite (COD) in human kidney stones. Such uncertainty stems from the failure to detect COT in voided human urine containing calcium oxalate crystalluria as well as from the results of studies carried out in vitro. These indicate that calcium oxalate crystallizes as COD and/or COM from solutions whose composition approaches that expected to be found at physiological conditions.

The hypothesis that the structural control of one phase facilitates the formation of another one is not novel in urolithiasis. Actually it has long been upheld (i.e., Lonsdale, 1968) that epitactic catalysis is of critical importance to the production of the various kidney stone-forming salts. This notwithstanding, the actual relevance of epitaxy in kidney-stone formation has never been demonstrated. Furthermore recent evidence discounts its importance in a number of kidney-stone associations specifically tested for evidence of epitaxial overgrowths (e.g.,Leusmann et al.,1984; Deganello and Chou,1984).

Therefore it is the purpose of this work to analyze at the atomic level the requirements necessary for COT to invert, respectively, to COD and COM. Furthermore the atomic constraints controlling the process of epitaxy in the association COM-COD will be first analyzed and then discussed in light of their clinical significance.

In an accompanying paper such approaches will be amplified to discuss the factors controlling the stability of COT and establish how and why selected inhibitors interact with its crystal structure as well as those of COD and COM.

## Results and Discussion

**Structure of COT.** For a detailed description of the crystal structure of COT the reader is referred to the specialized literature (Deganello et al.,1981). Here I report only enough data to clarify the ensuing discussion. Figure 1 shows that the bulk of the structure consists of dimers of calcium-centered polyhedra arranged according to triclinic symmetry ($P\bar{1}$). These dimers are made up by two monomers, each consisting of a polyhedron defined by one calcium atom and eight oxygen ligands. Of these eight oxygen ligands, three belong to water molecules. The remaining five ligands instead, partake in forming two oxalate groups. Adjacent dimers bridge with one another to form sheets by bonding with oxalate groups (marked with OX.1 in Fig. 1) and oxygen and hydrogen atoms from the water molecules. All of this results in large channels which delimit the hydrogen bond-network. Such channels are absent in COD and COM. Vertical continuity is assured by the juxtaposition of the sheets onto one another through selective bonding with another set of oxalate groups. These are perpendicular to their OX.1 counterparts.

**The phase change COT-COD.** If enough activation energy is available to disrupt the W(3)-W(1), O(2)'-W(1) and W(3)'-W(2) bond-configurations (Fig. 1), the oxygen ligands O(2) and W(3)'can coalesce onto, respectively, their W(3) and O(2)'counterparts (Fig. 2a). The resemblance of the ensuing atomic arrangement to that of COD (Fig. 2b) is patent even though no corrections have been made for the straitening of the structure. Adjacent dimers now share common atomic edges [the W(3)-O(2)'s in Fig. 1] with the result that the channels produced by the hydrogen bond-network are destroyed. Most of these changes can be readily appreciated even from the standpoint of the water molecules alone (Figs. 3,2a and 2b). It is not, in fact, topologically possible to proceed from COT to COD by condensation of atomic

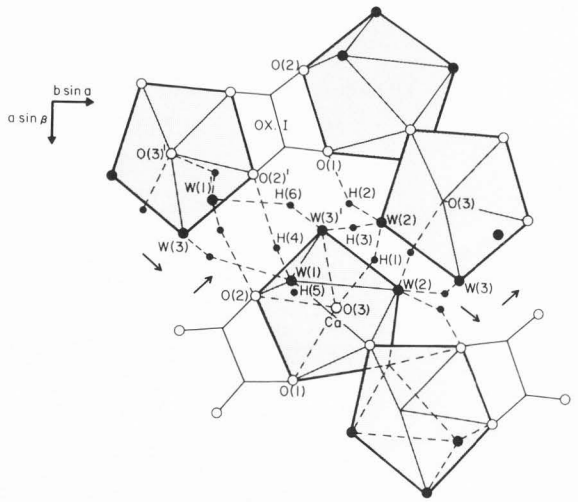
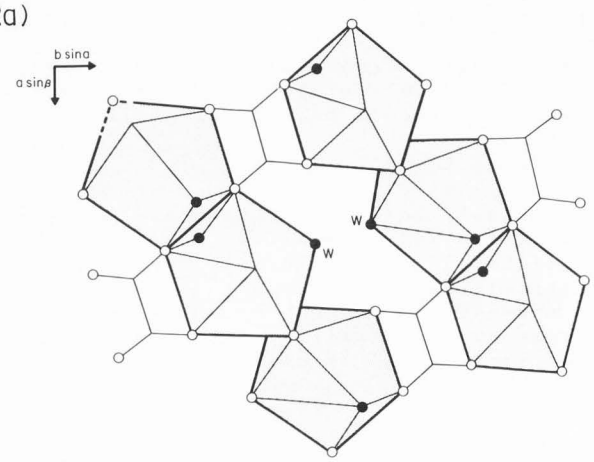
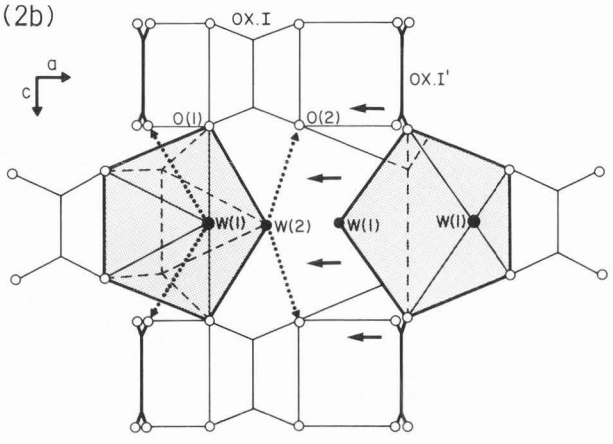



Fig. 1. Projection of the crystal structure of COT down [001]. Arrows indicate direction of open channels. Heavy dots represent water-oxygens (W's). Dashed lines show organization of latter ones. Ca stands for calcium atom. O's indicate oxygen ligands while H's are hydrogen atoms.

(2a)




(2b)




$CaC_2O_4 \cdot (2+X)H_2O$

Fig. 2a. Reconstruction of initial stages of COT-COD phase-transition. Heavy dots represent water-oxygens (W). Open circles stand for oxygen ligands. Notice that only two water molecules are available in each polyhedron.

Fig. 2b. A section of crystal structure of COD viewed down [010]. Heavy dots stand for water-oxygens. Open circles stand for oxygen ligands. Dotted lines indicate hydrogen-bond configuration. Notice that oxalate group OX.I'(in bold) is perpendicular to its OX.I counterpart which lays on plane of figure. Arrows indicate direction along which the calcium-centered polyhedra shift into their counterparts.

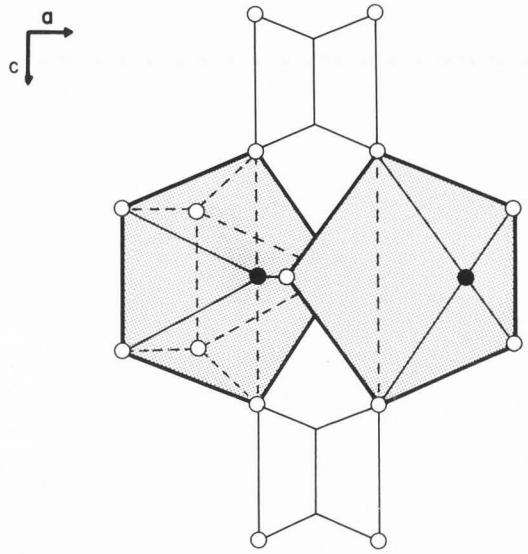



Fig. 3. Transition to COM. Two calcium-centered polyhedra (Fig. 2b) have shifted into one another. Consequenthly both share oxygens from the same oxalate group. Heavy dots represent water-oxygens. Open circles stand for oxygen ligands.

units already present since a significant rearrangement of the entire water-molecule configuration is necessary. In COD only two of the eight oxygens of the calcium-centered polyhedra belong to water molecules; the remaining ones, instead, partake in making four, rather than two, oxalate groups as is observed in COT. Because of the above and the elimination of the voids associated with the hydrogen bond-network, the structure of COD is more compact (specific gravity: 1.996 vs 1.887 g/cm$^3$ for COT) and more resistant to phononic and chemical destabilization.

COD crystallizes in a tetragonal space group (I4/m). It is likely that the process of phase transition COT-COD affects first the W(2)-O(3) (3.031 Å) and then the W(3)-W(1) (2.983 Å) bonds because of their longer length and thus, lower bond strength (Pauling, 1960). The phase change COT-COD is discontinuous or, according to the nomenclature of Buerger (1961), a reconstructive one.

**The phase-change COD-COM.** If the calcium-centered polyhedra shift into one another along the direction of the arrows (Fig.2b), the a axis shortens from 12.371 to 9.976 Å (Fig.3). In this process the bonding of the oxalate group OX.I' is disrupted and so are the W(1)-H(1)-O(2) and W(2)-H(2)-O(2) bonds. Consequently the structure distorts and organizes itself according to monoclinic symmetry (Fig. 4). Such a distortion is particularly efficient from the standpoint of the atomic packing since there is no empty space in COM. Accordingly, only one of the oxygen

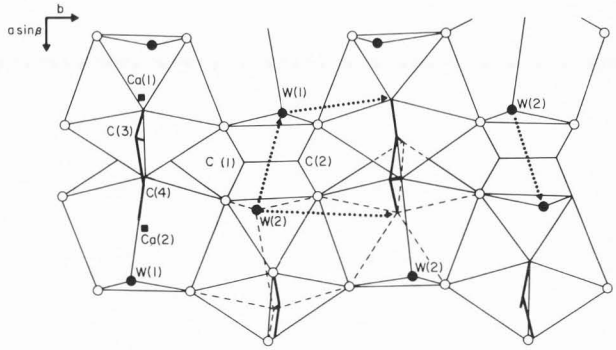



Fig. 4. A more complete view of the crystal structure of COM as seen down [001] ($P2_1/a$ setting). Dots represent water-oxygens; open circles show oxygen ligands; dashed lines stress architecture of water molecules; Ca stands for calcium atom. Notice that the C(3)-C(4) oxalate group (in bold) is perpendicular to its C(1)-C(2) counterpart which lays on plane of projection.

ligands bonds to a water molecule; the remaining seven, instead, are shared with five different oxalate groups. All of this results in planar sheets of calcium and oxygen atoms which juxtapose onto one another along the c axis. This juxtaposition is controlled by sets of C(3)-C(4)$O_4$ oxalate groups. These are perpendicular to their C(1)-C(2)$O_4$ counterparts laying on the plane of the sheets. Because of these changes COM gains in stability with respect to COD, measures higher specific gravity (2.21 g/cm$^3$), and tends to resist further dehydration. Actually, even if one manages to dehydrate COM to anhydrous calcium oxalate (alpha), this still retains an exceptional propensity to reacquire its pretransition configuration. Fig. 5 shows a Guinier-Lenne' photograph of anhydrous calcium oxalate taken under vacuum and at 70°C. As soon as either the vacuum or the temperature, or both are released, the structure instantaneously reverts to that of COM. Single-crystal photographs (precession camera) taken of anhydrous calcium oxalate using a heating device locally developed (Deganello,1982) confirm these results. At 90°C (40 kV, 20 mA, 18 h, $\mu$=20°, Zr-filtered Mo K$\alpha$ radiation), the x-ray reflections,

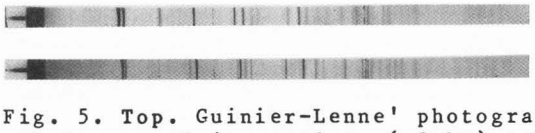


Fig. 5. **Top.** Guinier-Lenne' photograph of anhydrous calcium oxalate (alpha) taken at T=70°C and $10^{-2}$ Torr; (40 kV, 20 mA, 18 h; quartz monochromated Cu K$\alpha_1$ radiation). **Bottom.** As soon as either the vacuum or the temperature is released, the pattern instantaneously reverts to that of COM. Experimental conditions: same as above.

although well resolved, are nevertheless affected by a high degree of mosaicity in [001] projections. Extreme streaking and diffuseness instead affect the diffraction patterns of the [010]'s, thus indicating that those are the directions of maximum structural weakness. These data were confirmed with a four-circle automated diffractometer (Mo K$\alpha$ graphite-monochromated radiation) using a single crystal of COM heated at 90°C.

The COD-COM phase transition is discontinuous. Tomazic and Nancollas (1980) report a value of 2.26 (±0.2) kJmol$^{-1}$ for the driving force (-DG) of the transition, when measured in 0.15 M sodium chloride solution at T=37°C.

**The phase-change COT-COM.** If enough activation energy is available to shift the OX.I's in Fig. 1 from the O(2)-O(1) edges to those of the O(1)-W(2)'s, the dimers in COT acquire the bonding configuration found in COM. This raises an important consideration. The process of phase transition from COD to COM involves the breakage of two hydrogen bonds, the disruption of one oxalate group, and an overall reassessment of the topology of the calcium centered polyhedra. On the other hand, the phase-change COT-COM involves the breakage of three hydrogen bonds, the disruption of one oxalate group and a minor reorganization of the calcium-centered polyhedra. Consequently one must deduce that the energy necessary to invert COT directly to COM ought to be of the order of that required to transform COD to COM. This observation, based on the study of the values of the positional parameters does not take into account the effect of temperature. Table 1 reports the amount of motion which, because of temperature, each atom undergoes about its position. It is observed that the structure of COT is already seriously destabilized at room temperature. Not only are its oxygen ligands far more mobile than those of COD but so are its calcium and carbon atoms which make up the backbone of the structure. Unfortunately individual values of atomic thermal motion are not yet available at 37°C for either COT or COD; it is nevertheless expected that the trend reported in Table 1, although already highly significant, will become even more drastic as the temperature is increased. Such behaviour is expected to be accentuated in solution. Any change in temperature, in fact, increases the frequency of the modes of vibration of the molecules of the solution. This process, together with the atomic destabilization already taking place within the crystals, acts to synergistically reduce their structural stability as well as that of growing material. COT rather than COD is expected to be preferentially affected because of its weaker bonding and thus, higher

Table 1. Values of thermal vibration in COT and COD at room temperature.

| COT * | | COD ** | |
|---|---|---|---|
| Atoms | B(Å)$^2$ | Atoms | B(Å)$^2$ |
| Ca | 1.64 | Ca | 0.97 |
| O(1) | 3.41 | O(1) | 1.46 |
| O(2) | 3.36 | O(2) | 2.79 |
| O(3) | 3.79 | | |
| O(4) | 2.30 | | |
| C(1) | 2.93 | C | 1.23 |
| C(2) | 2.01 | | |
| OW(1) | 2.94 | OW(1) | 2.75 |
| OW(2) | 3.89 | OW(2) | 2.97 |
| OW(3) | 3.92 | | |

* Data from Deganello et al. (1981).
** Data from Tazzoli and Domeneghetti (1980).

Ca stands for the calcium atom while the O's and OW's represent, respectively, oxygens and water-oxygens. The C's stand for carbon atoms. The B's indicate the amount of movement which each atom undergoes around its centroid of revolution because of temperature.

solubility. One cannot escape the conclusion that the activation energy necessary to drive COT directly to COM at 37 °C must be lower than that required to induce the COD-COM transition. Furthermore, from a topological standpoint alone, a direct COT-COM transition is favored inasmuch as the organization of the calcium-centered polyhedra is remarkably similar in both structure types (Fig. 6). Those polyhedra, in fact, not only share a direct water-water correlation but a remarkable correspondence as well between the C(2)-C(2)$O_4$ oxalate group of one -(COT)- and the C(3)-C(4)$O_4$ oxalate group of the other. All of the above suggest that in solution a sequential phase transition according to the steps COT-COD-COM is not energetically favored. For this to occur COT should first change the organization of its polyhedra in order to accommodate them to the requirements of COD. Those polyhedra then would have to reorganize themselves back to a configuration remarkably reminiscent of the one which they already had before inverting to COD. It should be noticed that each time any of these reorganizations takes place energy must be provided to disrupt and properly reorganize at least one oxalate group.

Tomazic and Nancollas (1980;1979) report that the driving force for the COD-COM phase change (-DG=2.26 kJmol$^{-1}$; 37°C) is considerably less influenced by temperature than that of the COT-COM transition. For this they report that the

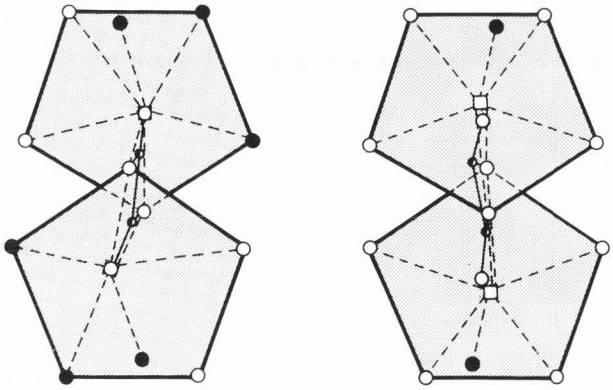



Fig. 6. Organization of interpenetrating Ca-centered polyhedra in COT (left) and COM. Dots stand for water-oxygens; open circles represent oxygen ligands; squares indicate calcium atoms. Dashed lines show bonding of calcium atom (partial). Hatched circles indicate carbon atoms.

driving force (-DG) increases from 2.4 to 3.58 $kJmol^{-1}$ between 15-50°C. At 37°C that is 3.06 $kJmol^{-1}$.

**Epitaxy in the COD-COM system.** Although a comparison between the structures of COD and COM does indeed suggest several similarities, it is not possible to identify any analytical relationship between the atomic coordinates of one structure and those of the other one (Tazzoli and Domeneghetti, 1980). This apparent impasse is solved once one realizes that COM, when properly ordered, ("basic structure"; Deganello 1980) has different symmetry (space group: I2/m) and length along the b axis (7.294 Å) than those routinely detected ($P2_1/n$; b=14.588 Å). A.S.T.M card nr.20-231 nevertheless reports a value of 7.294 rather than 14.588 Å for the b axis of COM. The error is caused by the procedure used (powder diffraction) which is not sensitive enough to detect weak reflections with k odd (Deganello, 1980). These arise because at physiological temperature atomic distortion and ordering cause two identical subcells of "basic" COM to slightly shift off register with respect to one another and link along b. The value of this axis is thus doubled while the overall diffraction pattern acquires several weak additional reflections. These are incompatible with the requirements of space group I2/m; instead, they reduce the symmetry to P21/n. Thus it follows that if one needs to make meaningful analytical comparisons, the atomic parameters of COD must be related to those of its undistorted parent structure, that is "basic" COM. This was done using the data for COD and "basic" COM reported by, respectively, Tazzoli and Domeneghetti, 1980, and Deganello and Piro, 1981. The results, reported in Table 2, are restricted to the 7.295 Å and (2 x) 6.291 Å axes of COM and their 7.357 Å and 12.371 Å counterparts of COD in order to avoid correcting for the shortening of a, which takes place during the COD-COM phase change. It is thus formally demonstrated that a considerable portion of the structure of COM (or COD) is essentially identical to that of COD (or COM). Those common atoms facilitate the transition of one phase into the other one as well as the formation of epitaxial overgrowths. This notwithstanding, here is not even implied that epitaxy must occur or is likely to occur in the COD-COM system. The existence of a close match in the values of two of their axial directions and the occurrence of atoms in essentially identical positions are, at best, a necessary but certainly not a sufficient condition for producing oriented overgrowths. Several additional constraints must be concurrently satisfied. In homoepitaxial systems (these are organizations in which the chemical composition of the substrate is essentially identical to that of the overgrowth) the most important of those are: (1) supersaturation of the solution from which the overgrowth is to crystallize; (2) feasibility of keeping that solution stationary; (3) undisturbed wetting of the substrate by the solution; (4) superior quality of the face of the substrate on which epitaxy is to occur and (5) absence of additives. As for (1), that requirement is almost certainly satisfied during the formation of kidney stones. It is in fact realistic to expect that the ion activity-product of kidney-stone formers surges to values ranging between those of the solubility and formation products of calcium oxalate. Compliance with (2), instead, is somewhat more difficult to rationalize. The growth of a renal stone, in fact, takes place under dynamic conditions. Even assuming that those approach steady-state level as,i.e., in an idealized renal system characterized by extreme constancy of renal blood flow, glomerulation filtration rate, and tubule water reabsorption, one would expect that the atomic bonds of the growing interfaces with the C's, W(1)'s, W(2)'s and O(1)'s should be disturbed by the dynamics of the urine flow. Point (3) requires that preformed seeds of calcium oxalate be anchored in the urinary system in a manner such that during epitaxial growth the faces acting as substrates remain perfectly stationary while they are exposed to supersaturated urine. Furthermore according to (4) the surfaces of those faces must be free of atomic defects since these favor the formation of multiple overgrowths having orientations of their own. Although one may foresee situations in which (3) might be operative, concomitant

Table 2. Coordinates of atoms common to COD and COM (basic).

| COM (basic) | | | COD | | |
|---|---|---|---|---|---|
| c=2 x 6.291 Å | | b= 7.295 Å | b=12.371 Å | | c=7.357 Å |
| Atoms | z/c | y/b | Atoms | y/b | z/c |
| C | 0.25 * | 0.116 | C | 0.241 | 0.105 |
| O(2) | 0.111** | 0.0 | OW(1) | 0.114 | 0.0 |
| O(W) | 0.022*** | 0.0 | OW(2) | 0.019 | 0.0 |
| O(1) | 0.195 | 0.184 | O(1) | 0.246 | 0.183 |

* or 0.5 of 6.291 Å.
** or 0.212 of 6.291 Å
*** or 0.044 of 6.291 Å.

C stands for carbon atoms while the O's and the O(W)'s represent, respectively, oxygens and water-oxygens.

COM (basic): a= 9.978 Å; b= 7.295 Å; c= 6.291 Å

COD: a=b= 12.371(3) Å; c= 7.357(2) Å.

compliance with (4) appears to be a considerably less likely event. As to (5), this poses a formidable demand. Many chemical species besides calcium and oxalate are present in urine. These molecules are, at the very least, adsorbed onto either the crystals of COD or COM. Adsorption of impurities is bound to either halt nucleation altogether and/or foster the occurrence of nucleation centers characterized by orientations incompatible with those of their substrates. As shown by Joyce et al., (1967), crystalline growth in homoepitaxial systems is characterized by an induction period during which it is operative only at highly selected sites. No other nucleation centers can develop during this period. Only when those initial three-dimensional nuclei have grown large enough to coalesce, thus forming a continuous layer over the substrate, can the epitaxial interfaces continue to grow. Looking from another perspective, the findings of Joyce et al., become self-explanatory, if one considers that the interface where epitaxy takes place must have its atomic structure in register with that of the developed overgrowth. The binding of impurities to those very atoms where growth is supposed to commence, adversely affects local structural stability.

All of the above indicates that epitactic catalysis cannot and should not be regarded as an ubiquitous and common mechanism for the production of kidney stones in general and of COM from COD (or vice versa) in particular. It should be noted that in supersaturated urines, as are, at one time or another, those of kidney stone-formers, one would expect that the reaction rate, which controls the reactions occurring on or near growing interfaces, should be faster than the growth rate. This is operative only as a selective process of addition of atoms to specialized surfaces. Consequently, in supersaturated urines excess atoms are available to form nuclei and, thus, crystallites exhibiting growth orientations incompatible with those expected from an epitaxial overgrowth. An extreme case and point is the association COM-uric acid. Oriented overgrowths of COM can indeed be produced onto substrates of uric acid (Deganello and Coe,1983), but only with great difficulty. On the other hand, human "mixed" stones of COM and uric acid, although common, fail to provide any evidence of epitaxy (Deganello and Chou, 1984).

## Acknowledgments

Grant AM 33949 from the National Institutes of Health is acknowledged. Dr.F.L. Coe kindly read the manuscript. A special appreciation goes to Professors Jacobson and Horner who, as outside referees, greatly helped in editing the vagaries of my English.

## References

Buerger MJ.(1961).Polymorphism and phase transformations. Fortschr. Mineral. 39,9-24.

Deganello S.(1980). The basic and derivative structures of calcium oxalate monohydrate. Z.Kristallogr. 152, 247-252.

Deganello S.(1982). A holder for high T/P cells in four-circle diffractometry. N.Jb.Miner., H.6, 287-288.

Deganello S, Chou C.(1984). The uric acid-whewellite association in human kidney stones. Scanning Electron Microsc. 1984;II: 927-933.

Deganello S, Coe FL.(1983). Epitaxy between uric acid and whewellite: experimental verification. N.Jb.Miner., H.6, 270-276.

Deganello S,Piro OE.(1981). The crystal structure of calcium oxalate monohydrate. N.Jb. Miner., H.2,81-88.

Deganello S, Kampf AR, Moore PB.(1981). The crystal structure of calcium oxalate trihydrate. Amer. Miner. 66,859-865.

Gardner GL. (1975). Nucleation and crystal growth of calcium oxalate trihydrate. J.Cryst. Growth 30,158-168.

Joyce BA, Bradley RR, and Booker GR. (1967). A study of nucleation in chemically grown epitaxial silicon films using molecular beam techniques. III. Nucleation rate measurements and the effect of oxygen on initial growth behaviour. Phil. Mag. 15,1167-1187.

Leusmann DB, Meyer-Jurgens U-B, Kleinhans G.(1984). Scanning electron microscopy of urinary calculi-Some peculiarities. Scanning Electron Microsc. 1984;III: 1427-1432.

Lonsdale K.(1968). Epitaxy as a growth factor in urinary calculi and gallstones. Nature 217, 56-58.

Pauling L.(1960). The nature of the chemical bond. Pgs. 505-562, Cornell Univ. Press.,Ithaca, NY.

Tazzoli V, Domeneghetti C.(1980). The crystal structures of whewellite and weddellite: re-examination and comparison. Amer. Miner. 65, 327-334.

Tomazic BB, Nancollas GH.(1979). A study of the phase transformation of calcium oxalate trihydrate-monohydrate. Inv. Urol. 16, 329-335.

Tomazic BB, Nancollas GH.(1980). The kinetics of dissolution of calcium oxalate hydrates. II. The dihydrate. Inv. Urol., 18, 97-101.

## Discussion with Reviewers

**D.B. Leusmann:** In urinary calculi, one frequently finds pseudomorphs of COM after COD. Did you perform precession or Weissenberg-photographs of those partly transformed crystal aggregates and did they confirm your suggestions?
**Author:** No, I did not. I should stress, however, that only complete structural determinations of mixed-phase single crystals, and not the taking of selected projections, are necessary to identify individual atoms.

**B. Tomazic:** The author implies that COT-COM transformation may be more accentuated by the presence of urine (and/or solution). The experimental evidence (Tomazic and Nancollas, 1979) proves just opposite: COT transformation is markedly retarded by selected inhibitors and in urine solutions. It is not conceivable that the minute concentrations of inhibitors would freeze the amount of atom motion (Table 1). What other mechanism can be suggested for the remarkable stabilization of COT?
**Author:** The implication is that, in general, the indiscriminate addition of foreign chemical species to a solution from which COT grows, is likely to disturb the growth of the latter. As a general rule, in order to protect COT stability, one must be able to preserve its structural integrity. This can be achieved by adding to the solution from which COT crystallizes minor amounts of selected inhibitors ("dopants") which are found to be effective in this process. However, the mechanism required to increase and/or preserve stability is not likely to be one of simply freezing atomic motion even though such an occurrence would eventually be a necessary byproduct. At the very minimum the foreign atoms are likely to organize specific bonding interactions with the structure of COT in order to stabilize it. They also cause the solution to minimize the number of calcium atoms that bond with the oxalic groups. As for urine, that contains some of those dopants and a glycoprotein which inhibits the growth of calcium oxalate. It would therefore appear that their synergistic interaction is such that, under the conditions referred to by the reviewer, growth of COD and COM is minimized.

**B. Tomazic:** Which mechanism is operative for the suspension transformation of calcium oxalate hydrates? The difference in driving forces for a phase change arises from the difference in solubilities

of COT and COD compared to COM,suggesting the dissolution/reprecipitation transformation mechanism, which was experimentally documented (Tomazic and Nancollas,1979; 1980). This appears to be in disagreement with the author's concept of structural collapse of COT to form COM, which probably suggests topotactic transformation.

**Author:** No, there is no fundamental disagreement. Whenever a set of primary bonds such as,i.e., those coordinating the calcium atoms, the hydrogens or the oxalate groups, are breaking apart,the structure commences to collapse. This can be a short as well as a long-range effect. Eventually in the solid state this results in polycrystalline material having the properties of the new phase. In solution, that collapse coincides with the various stages of dissolution. Consequently the resulting solute reorganizes itself according to the physico-chemical requirements of the solution since those dictate the nature of final phase formation. In particular the structural requirements of the hydrates of calcium oxalate indicate that in order for each of them to achieve phase stability, it is necessary, although not sufficient, that a proper ratio of calcium atoms is kept with respect to the oxalate groups. In COT each calcium atom shares oxygens with two different oxalate groups; in COD and COM, instead, each calcium atom bonds to four and five oxalate groups, respectively. Therefore the attainment of individual phase stability requires a precise regulation of calcium and oxalate supply. Any change in the kinetics of delivery of either one can result in structural instability and,thus, cause a phase transition to a lower and more stable phase. Obviously temperature and the presence of dopants can either stabilize and/or maximize these effects.